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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,482	09/15/2000	Linda Anne Crofts	1871-130	9624

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EXAMINER
ULM, JOHN D

ART UNIT	PAPER NUMBER
1646	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/509,482	Applicant(s) Crofts et al.
	Examiner John Ulm	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6)\MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 11, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above, claim(s) *5-8, 15-20, and 25* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 9-14, and 21-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

1) Claims 1 to 25 are pending in the instant application. Claims 1, 10 and 17 have been amended as requested by Applicant in Paper Number 8, filed 11 February of 2002.

2) The drawings in the instant application do not comply with 37 C.F.R. § 1.821(d), which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. M.P.E.P. 2422.02 expressly states that "when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings". Figure 1 of the instant specification, for example, depicts three amino acid sequences without employing the required sequence identifiers to describe them.

3) The instant specification does not comply with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For example, lines 31 and 32 on page 11 of the instant specification discuss two PCR primers without employing the required sequence identifiers. Correction is required. See M.P.E.P. 2422.03.

4) The instant specification does not comply with 37 C.F.R. § 1.84(U)(1), which states that partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. Figure 5 of the instant application, **for example**, is presented on four separate panels. The

four sheets of drawings which are labeled " Figure 5" in the instant specification should be renumbered "Figures 5A, 5B, 5C and 5D". Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

5) This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

6) The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

7) Claims 5 to 8, 15 to 20 and 25, as well as claims 1 to 5, 9 to 14 and 21 to 24 in so far as they are drawn to complementary nucleic acids, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8. The traversal is on the ground(s) that a transgenic animal comprising a polynucleotide should not be distinguished from a host cell containing that same polynucleotide. This is not found persuasive because M.P.E.P. 803 states that:

" For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant."

Serious burden was shown in the original requirement by the separate classification and separate status in the art of the different inventions. Applicant has provided neither a showing or evidence to the contrary. Further, Applicant's argument that a polynucleotide and its' complement are capable of use together ignores the breadth of Applicant's probe claims, which only require 10 nucleotide bases. These different nucleic acids lack a common utility because a nucleic acid encoding a protein can not be employed to detect a corresponding mRNA in a sample and the complement of that nucleic acid can not be employed to produce a protein. Because each is not required for the other, a polynucleotide and its' complement are distinct chemical compounds. The argument that a polynucleotide and its complement are not distinct because they can form a complex is not persuasive because the same argument can be made for a receptor and a ligand, an antibody and an antigen, and an enzyme and substrate, and yet a receptor is usually chemically distinct from a ligand thereto, as is a antibody and antigen as well as an enzyme and substrate. Therefore, the simple fact that two compounds are capable of forming a complex is not a basis for the conclusion that those two compounds are patentably indistinct.

The requirement is still deemed proper and is therefore made FINAL.

8) Claim 1 is objected to as reciting an improper Markush Group because a polynucleotide and its complement lack a common utility which is based upon a shared structural feature. Claims 21 to 24 are also objected to as reciting an improper Markush Group for those reasons of record on page 2 of Paper Number 7. Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9) Claims 1 to 4 and 9 to 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims encompass a polynucleotide molecule comprising a nucleotide sequence from the genus of nucleotide sequences encompassed by the limitation "a sequence that substantially corresponds or is functionally equivalent to that of exon ad of the human VDR gene". The only member of that genus of nucleotide sequences which is described in the instant specification in sufficient detail to demonstrate possession is SEQ ID NO:1. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. ,

107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of a single member of the claimed genus, it does not describe a representative number of species within that genus, "by structure, formula, chemical name, or physical properties", to show possession of the genus. *In re Clarke*, 148 USPQ 665, (CCPA 1966) held that;

" It appears to be well settled that a single species can rarely, if ever, afford support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.21 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on

the circumstances of particular cases. Thus, in the case of a small genus such as halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably large number of reductions to practice would probably be necessary."

10) Claims 1 to 4 and 9 to 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make use the invention. These claims encompass an isolated polynucleotide "that substantially corresponds or is functionally equivalent to" SEQ ID NO:1 of the instant application. The limitations "substantially corresponds" and "functionally equivalent", as defined on page 7 of the instant specification, allow for changes in the nucleotide sequence of SEQ ID NO:1 so long as those changes do not effect functionality. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other

embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

The instant specification only provides single, naturally occurring example of the claimed polynucleotide. The instant specification does not disclose a specific, assayable function for that single polynucleotide. And, most significantly, the instant specification does not identify those nucleotide in SEQ ID NO:1 which are believed to be critical to the function of that polynucleotide and those bases which are expendable. Further, the instant specification does not identify an analogous polynucleotide in the prior art for which this information is known and could be applied to a polynucleotide of the instant invention by extrapolation. Because the instant invention provides neither working examples or guidance, one can not alter SEQ ID NO:1 at even a single base and predict "by resort to known scientific law" if the altered polynucleotide will retain functionality.

11) Claims 21 to 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. Whereas one could readily make a polynucleotide having at least 75% sequence identity to SEQ ID NO:1, the only specific utility disclosed for the claimed polynucleotide is in a process of producing alternatively spliced forms of a human vitamin D receptor, and the only polynucleotide described in the instant specification which functions in this capacity is SEQ ID NO:1. As

indicated in the preceding paragraph, one could not alter SEQ ID NO:1 at even a single nucleotide base by following the guidance provided by the instant specification and predict that the resulting polynucleotide can be employed in the disclosed process.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12) Claims 1 to 4, 9 to 14 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are vague and indefinite because of the presence of the limitations "functionally equivalent" and/or "substantially corresponds". Page 7 of the instant specification defines the term "functionally equivalent" in vague language such as "which encode VDR isoforms of substantially equivalent biological activity". This is particularly confusing because Figure 1 of the instant application appears to indicate that SEQ ID NO:1 lies in a 5' non-coding region of a vitamin D gene and, therefore, encodes nothing. The term "substantially corresponds" is vague and indefinite simply because one can not determine at what point in divergence two similar polynucleotide sequences would cease to "substantially correspond".

13) The prior art of record did not disclose or suggest an isolated polynucleotide comprising SEQ ID NO:1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1800